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| 10/584,113 | 04/04/2007 | Kristian Lund Henriksen | BECK:001 | 3904 |

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| EXAMINER | |
|---|---|
| SCHUBERG, LAURA J | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/584,113 | HENRIKSEN ET AL. | |
| | Examiner | Art Unit | |
| | LAURA SCHUBERG | 1657 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 January 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-50* is/are pending in the application.

4a) Of the above claim(s) *12-18,27-31,and 49* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11,19-26,32-48 and 50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/19/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

This action is directed to papers filed 01/19/2010.

Claims 1-50 are pending. No claims have been amended, newly canceled or newly amended.

Claims 12-18, 27-31 and 49 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected specie, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 07/24/2009.

Claims 1-11, 19-26, 32-48 and 50 have been examined on their merits.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

### *Oath/Declaration*

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:
It does not identify the mailing address of each inventor. A mailing address is an address at which an inventor customarily receives his or her mail and may be either a home or business address. The mailing address should include the ZIP Code designation. The mailing address may be provided in an application data sheet or a supplemental oath or declaration. See 37 CFR 1.63(c) and 37 CFR 1.76.

The mailing address is missing for the third listed inventor (Marianne Winning).

## *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1, 3-11, 19-26, 33-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Giagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS).**

Claim 1 is drawn to a probiotic tablet comprising at least two zones wherein the first zone comprises a probiotic and a second zone comprises at least one other active ingredient kept separate from the probiotic in the first zone and wherein the water activity of the probiotic in the first zone is no greater than 0.2 and the water content of the tablet being no less than 0.2% by weight.

Dependent claims include wherein the first zone is free from amounts deleterious to the viability of the probiotic of several ingredients (claims 3-10), wherein the second zone contains iron as an active ingredient (claims 11 and 19), the addition of a desiccant carrier material (claims 20-22), a multi-layer structure (claim 23), first zone free of encapsulated iron , zinc and copper (claims 24-26), specific water contents (claims 33-39), specific water activity (claims 40-44), a water excluding barrier material surrounding the first zone of the tablet (claim 45), including a tablet coating that

excludes water (claim 46) and wherein the tablet is stored under specific conditions (claim 47) and wherein the barrier material is a fat or wax based material (claim 48).

Giagau et al teach a two-part micronutrient product, useful as a dietary supplement and for treatment of disease which comprises a probiotic component and secondary ingredients in another component (abstract). The product may be formulated as multi-component single tablet (page 5, 4th paragraph) and includes wherein the first and second components are kept separate from each other (page 2, 5th paragraph). The second portion is taught to potentially contain many different secondary ingredients and includes combinations of iron and vitamins B6 and C (page 8). Adjuvants to be added to the probiotic include starch (page 8 example 1) and other ingredients that improve the bioavailability and shelf life of the probiotic (page 6, 1st paragraph). The first component is kept free of amounts of any substances that are deleterious to the viability of the probiotic.

Giagau et al do not appear to explicitly describe a zoned single tablet.

Bakulesh et al teach a method of making a pharmaceutical tablet formulation of a probiotic that is kept separate from secondary active ingredients by the addition of barrier materials (page 13). This is interpreted as a multi-zoned tablet. Exemplary barrier materials are taught to include oil/wax based materials (page 15, number 9).

It would have been obvious to make a multi-zoned single tablet for the product of Giagau et al. One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success because Bakulesh et al teach that it is known in the art to formulate a probiotic tablet with barrier materials to keep the primary ingredient of

the probiotic separate from the potentially deleterious secondary ingredients. One of ordinary skill in the art would have been motivated by the teachings of Giagau et al as well since this reference includes a formulation of the multi-component product that includes the form of one tablet (page 5 4th paragraph) as well as the need to keep the probiotic separate from the nutrients in the second component (page 2 paragraph 5).

Giagau et al are silent with regard to the water content and water activity of the probiotic composition.

Runge et al teach dried microorganism cultures that are compressed and used for foodstuffs and feedstuffs (abstract). Preferred probiotics include Lactobacillus sp. As well as other genera (column 6 lines 19-44 of US 7,037,708). Dry preparations having low moisture content (of from about 2 to 3% by weight of water) corresponding to a water activity of from 0.03 to 0.15 are provided by spray drying and have survival rates of up to 60% after storage for 1 year at ambient temperatures and ambient air conditions (column 5 lines10-21). Tablet formulations of the dried microorganisms are taught as suitable and include the addition of tabletting aids such as PVP (column 11 lines 47-67) and desiccants (column 10 lines 8-18). Coating materials are added to hinder the ingress of moisture to the dry preparation (column 12 lines 24-26). Storage in suitable containers is taught as well (column 18 lines 1-10).

It would have been obvious to apply the formulation methods of Runge et al to the tableted probiotic composition of Giagau et al with regard to the water content, water activity and suitable additives of the different zones. One of ordinary skill in the art would have been motivated to do so because Runge et al teach that these parameters

are beneficial to the viability and shelf life of a dried probiotic composition. Modifying the water activity to 0.02 would have been a matter of routine optimization and experimentation as the artisan of ordinary skill would be motivated to attain a dry microorganism with the greatest stability and viability. The use of a storage container with a desiccant would have also been obvious as Runge et al teach the benefit of adding desiccant materials and storing the product in suitable storage containers as well. One of ordinary skill in the art would have had a reasonable expectation of success because both Giagau et al and Runge et al are producing tableted probiotic compositions for oral administration.

Therefore the combined teachings of Giagau et al, Bakulesh et al and Runge et al render obvious Applicant's invention as claimed.

**Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Giagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Belicova et al (Folia Microbiol. 2004).**

Claim 2 includes wherein the first zone also contains selenium as an additional active agent.

The combined teachings of Giagau et al, Runge et al and Bakulesh et al render obvious the claimed invention as described above, but do not specifically include wherein selenium is included in the first zone with the probiotic component.

Belicova et al teach that the antimutagenic activity of probiotic bacterium *Enteroccus faecium* was enhanced by the addition of selenium. Selenium enriched probiotic bacterium *E. faecium* can be considered as a food supplement with beneficial health benefits (page 304, last paragraph).

Therefore it would have been obvious to include selenium in the first zone with the probiotic component of the Giagau et al composition because Belicova et al teach that selenium enhances the antimutagenic activity of probiotic bacterium *Enteroccus faecium* and selenium enriched probiotic bacterium *E. faecium* can be considered as a food supplement with beneficial health benefits (page 304, last paragraph). One of ordinary skill in the art would have had a reasonable expectation of success because Giagau et al were also using the probiotic bacterium *Enteroccus faecium* as well (page 2, last paragraph).

Therefore the combined teachings of Giagau et al, Runge et al, Bakulesh et al and Belicova et al render obvious Applicant's invention as claimed.

**Claims 32 is rejected under 35 U.S.C. 103(a) as being unpatentable over Giagau et al (DE 10206995 machine translation) in view of Runge et al (WO**

**99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Andoh et al (EP 0255725).**

Claim 32 includes wherein the tablet has a multitude of granules constituting the first zone surrounded by a matrix, and wherein the matrix constitutes a second zone **or** wherein the matrix also contains a multitude of granules constituting the second zone.

The combined teachings of Giagau et al, Runge et al and Bakulaesh et al render obvious the claimed invention as described above, but do not specifically include a formulation that includes zones of matrix and compressed granules. However, Giagau et al do indicate that additives that offer an improvement or benefit to the final product formulation may be included (page 6).

Andoh et al teach a sustained release multi-granule tablet useful in the field of therapy. The invention is concerned with a tablet of the multiple unit type (different zones) in which sustained release granules are contained as a unit (page 2, 1st paragraph). Water resistant coatings (barriers) are applied in layers between the different zones (page 3).

Therefore one of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the formulation strategies of Andoh et al to the probiotic tablets of Giagau et al because Andoh et al teach that these are suitable for the formulation of multi-component tablets for pharmaceutical use.

Therefore the combined teachings of Giagau et al, Runge et al, Bakulesh et al and Andoh et al render obvious Applicant's invention as claimed.

**Claim 50 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Giagau et al (DE 10206995 machine translation) in view of Runge et al (WO 99/57242-using US 7,037,708 as translation) and Bakulesh et al (GB 2323532- from IDS) as applied to claims 1, 3-11, 19-26, 33-48 above, and further in view of Cavaliere et al (EP 0956858- from IDS).**

Claim 50 includes wherein the first zone disintegrates at a faster rate than the second zone and is no more than 50% of the total disintegration time.

The combined teachings of Giagau et al, Runge et al and Bakulesh et al render obvious the claimed invention as described above, but do not specifically include different disintegration times of the different zones. Giagau et al do indicate that additives that offer an improvement or benefit to the final product formulation may be included (page 6) and Runge et al indicate that formulating the product to allow for a more rapid release of the microorganism is suitable as well (column 11 lines 7-45).

Cavaliere et al disclose a two-layer tablet comprising a quick release layer and a slow release layer, both containing a dried probiotic culture. The quick release layer disintegrates in a lapse of time of 10-25 minutes whereas the slow release layer disintegrates in a lapse of time of 25-50 minutes (page 4 paragraphs 28-29).

Therefore one of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the formulation strategies of Cavaliere et al

to the probiotic tablets of Giagau et al because Cavaliere et al teach that these are suitable for the formulation of multi-component probiotic tablets for pharmaceutical use.

Modifying the release characteristics of the tablet in order to optimize the therapeutic result would have been a matter of routine optimization and experimentation, the artisan of ordinary skill motivated to release the probiotics in a manner that increases the effectiveness of the probiotic microorganisms.

Therefore the combined teachings of Giagau et al, Runge et al, Bakulesh et al and Cavaliere et al render obvious Applicant's invention as claimed.

## ***Response to Arguments***

Applicant's arguments with respect to claims 1-11, 19-26, 32-48 and 50 have been considered but are moot in view of the new ground(s) of rejection. Applicant's arguments have been addressed in so far as they relate to the new grounds of rejection above.

Applicant has filed a new machine translation for the German patent DE 10206995 that was cited in the last office and also above. Applicant asserts that the new translation is more accurate than the previously cited one.

This is not found persuasive because the translations appear very similar. However, since there appears to be some disagreement as to the translation of this

German Patent a full human translation has been ordered and will be filed at a future date if needed.

Applicant argues that the teaching of the Runge reference is limited to those compositions that contain probiotics with non-deleterious ingredients. Applicant asserts that the skilled reader does not learn that the water content and the water activity disclosed in Runge et al is relevant to the problem of storage of probiotic micro-organisms in the presence of nutritionally active materials.

This is not found persuasive because the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). As long as the optimum water content and water activity are disclosed as being beneficial for a dried probiotic-containing composition one of ordinary skill in the art would have sufficient motivation and reasonable expectation of success to apply this teaching to all dried compositions that contain probiotics.

Applicant argues that the Giagau reference teaches away from formulating the probiotic and the nutrients into a single tablet. Applicant asserts that there is no disclosure of a single tablet unit containing both of the product portions.

This is not found persuasive because Giagau does in fact explicitly teach wherein the formulation of the combination product includes a single tablet. Giagau explicitly teaches wherein "the Probiotika contained micro nutrient combination product of comprising at least two products with different composition is present in the form of 0 to

10 tablets, preferably 1 to 5 tablets" (see page 5 paragraph 4). While the reference does suggest that the ingredients can be dispensed separately, this disclosure clearly includes a probiotic nutrient combination formulated as 1 tablet as well.

## *Conclusion*

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to LAURA SCHUBERG whose telephone number is (571)272-3347. The examiner can normally be reached on Mon-Fri 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura Schuberg
Examiner
Art Unit 1657

/Laura Schuberg/